Innovative method and installation for heating and melting bases for the production of suppositories

Oleksii Shmatok[1], Olesya Stepanova[1], Rostislav Bazeev[1]

1. Institute of Engineering Termophysics of National Academy of Sciences of Ukraine,
Kyiv 03057, Zhelyabov str. 2-a, e-mail: htplab@ukr.net

Abstract – The method for the thermal contact heating and melting of ointment bases for the manufacture of soft dosage forms at pharmaceutical companies is presented and the installation for its implementation is developed.

Keywords – heat exchange processes, heating, melting, ointment base, intensification.

Introduction

Suppositories are becoming more common in pharmacy and medicine due to the high rate of absorption of drugs and the possibility of combining ingredients with different pharmacological, physical and chemical properties in suppositories. Suppository dosage forms (DF) in the pharmaceutical market of Ukraine are now represented in most foreign pharmaceutical companies (leaders are from: Germany, France, Italy and Switzerland) and a small number of domestic companies: Lekhim (Kharkiv), Monfarm (Monastyrishche), “FITOLEK” (Kharkiv), Sperko Ukraine (Vinnitsa), Pharmex Group (Borispol) [1]. Out-of-date technologies and equipment for the manufacture of suppositories are the reason for the purchase and operation of imported equipment from Germany, Italy, the USA and other countries. The necessity for development and implementation high-performance innovative technologies and equipment for the production of suppository dosage forms (DF) is due to the demand of the people in domestic pharmaceutical preparations.

Main material

Suppositories from the physico-chemical point of view are considered as dispersed systems consisting of a dispersed medium, represented by a base, and a dispersed phase, in the role of which medicinal substances act. Suppositories are complex multicomponent heterogeneous systems, since they contain one or more drugs dispersed or dissolved in a simple or complex basis.

The technology of production of suppository DF includes a complex of heat and mass transfer processes: heat transfer during heating, cooling and melting; stirring and dissolving; dispersion (increase of phase interface) and homogenization; structuring (obtaining a bundle-disperse system); extraction (convective and molecular diffusion, as well as transfer of matter from solid to liquid phase).

An important stage for obtaining suppository DF is the preparation of suppository bases. Hydrophobic and hydrophilic bases and their mixtures are used depending on the pharmacological action of suppositories. Some problems arise when obtaining stable diphilic bases containing hydrophilic and hydrophobic parts, but such bases give the opportunity to introduce into them both fatty and water-soluble medicinal substances and their solutions.

The importance and role of the bases for suppositories are important and diverse. The bases provide the necessary mass of suppositories and, accordingly, the proper concentration of medicinal substances, a soft consistency, significantly affect their stability. The degree of release of drugs from suppositories, the speed and completeness of their absorption in many respects depend on the nature, composition and properties of the base.

Reactors with different types of mixers (Fig. 1, a), bathtubs with coils (Fig. 1, b), electric heaters, heating chambers, etc. are used according to the traditional technology for heating and melting of bases in pharmaceutical factories. But these methods have a number of significant disadvantages: labor-intensive and energy-consuming; possible overheating of the base, which leads to various changes in the physical-chemical and structural-mechanical properties of the dispersion phase; occurrence of contamination; not uniform heating of the whole mass of the base. For example, overheating of fats and fatty substances often leads to the formation of such forms that have lower melting temperatures, as well as suppositories after overheating of the base are unstable during storage, since they are melted at room temperature. In this case, the substances lose their hardness, which excludes the possibility of manufacturing suppositories.

A method of thermal contact melting through contact and convective heat transfer, which allows to intensify the process and reduce energy costs is developed in the Institute of Engineering Termophysics [2-4]. The principle of the method for melting the suppository base in cylindrical container is on the movement of the heating disc under the action of gravity during the melting and flow of the molten base through the gaps between the disc and the walls of the container. The difference between the proposed method and the existing one is to bring energy directly to the front of the phase transformation with the help of the heating disc that contacts the outer boundary of the unmelting substance. The method allows to heat and melt only that part of the base, which is necessary. It is possible to realize the controlled melting process, which enables more efficient use of energy. In this case, the temperature of the disc heater in the base contact area is lower than the temperature of its destruction. The melting occurs due to convective heat transfer from the upper surface of the heater in the molten mass.

An installation for thermo-contact heating and melting was developed on the basis of the proposed method (Fig. 1, c). The installation combines three technological operations: melting, unloading and dosage, and besides energy efficiency, can save time and human resources.

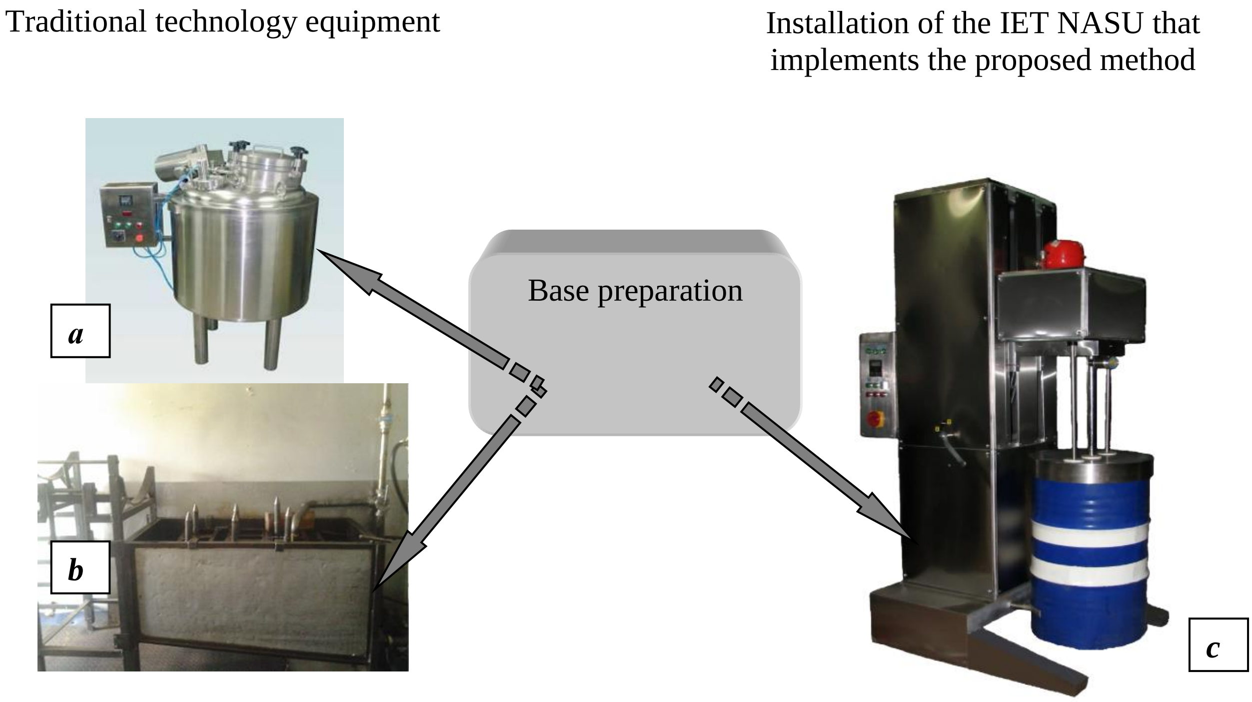
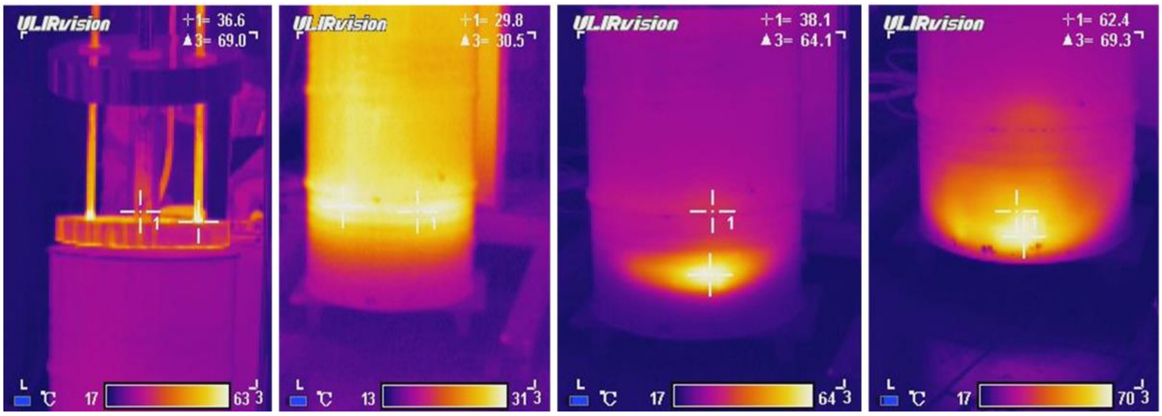


Fig.1. Equipment for heating and melting bases for the manufacture of suppositories:
a) a reactor with a mixers; b) bathtub with coil; c) “Thermobat” type installation.

Using thermal imager Ti-160 it was possible to trace the movement of the heater along the length of the container, as well as the temperature distribution on the surface of the thermo-contact heater and inside the metal drums of the manufacturer (Fig. 2). Thermograms show uniform heat-up of the thermo-contact heater (Fig. 2, a) and the total volume of the melt as it moves to the bottom of the drum and melt the base (Fig. 2, b-d). Due to the low coefficient of thermal conductivity, the base is in the initial viscous state, and it is heated and melted in contact with the heater (Fig. 2, c). At the end of the process (Fig. 2, d), convection flows are observed, which helps maintain the temperature of the melt at a given level.



a) b) c) d)

Fig. 2. Thermograms of thermo-contact heating process and melting of bases in the drums of the manufacturer:

a) heat up of the thermo-contact heater; b) the beginning of heating and melting; c) heating in the process of lowering the thermo-contact heater; d) the end of heating and melting (the thermo-contact heater drops to the bottom of the drum).

The developed method and the installation for thermo-contact heating and melting allow to melt the required amount of base quickly and efficiently (Figs. 3 and 4) for transportation to the next stages of the manufacture of suppositories. “Thermobat” type installation, which correspond to GMP standards, was developed and implemented at pharmaceutical factories: UC “Pharmacy”, “Lugansk Pharmaceutical Factory”, Lugansk; JSC “Riga Pharmaceutical Factory”, Riga; LLC “Ternofarm”, Ternopil.

Fig. 3. White pharmaceutical vaseline MERKUR 500 (Germany).

Fig. 4. Molten vaseline on installation “Thermobat -M”.

References

1. I.M. Pertsev, V.V. Postol’nyk, and O.L. Khalyeyeva, “Suppository drugs on the market of Ukraine”, *Visnyk farmatsiyi*, no. 1, pp. 43-49, 2001.

2. L.M. Grabov, V.I. Merschiy, V.N. Vashchenko, and T.V. Pisarenko, “Optimization process of thermal contact melting of materials”, *Promyshlennaya teplotekhnika*, vol. 22, no. 1, pp. 94-99, 2000.

3. L.M. Grabov, V.I. Merschiy, and S.I. Bondar, “A method of melting substances and device for its implementation”, UA Patent 31435, 17 Dec., 2001.

4. A.A Dolinsky., L.M. Grabov, and O.E. Stepanova, “Heat transfer at heating and fusion of bases for manufacturing of cosmetic and pharmaceutical preparations”, *Promyshlennaya teplotekhnika*, vol. 33, no. 3, pp. 12-19, 2011.